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SEQUENCE LISTING

<110> TRANSGENE S.A.

<120> Novel multifunctional cytokines

<130> TG163

<160> 59

<170> PatentIn version 3.1

<210> 1

<211> 345

<212> PRT

<213> artificial sequence (fusion human IL-7/linker/human IL-2)

<400> 1

Met	Phe	His	Val	Ser	Phe	Arg	Tyr	Ile	Phe	Gly	Leu	Pro	Pro	Leu	Ile
1									5		10				15

Leu	Val	Leu	Leu	Pro	Val	Ala	Ser	Ser	Asp	Cys	Asp	Ile	Glu	Gly	Lys
								20	25				30		

Asp	Gly	Lys	Gln	Tyr	Glu	Ser	Val	Leu	Met	Val	Ser	Ile	Asp	Gln	Leu
									35	40			45		

Leu	Asp	Ser	Met	Lys	Glu	Ile	Gly	Ser	Asn	Cys	Leu	Asn	Asn	Glu	Phe
								50	55			60			

Asn	Phe	Phe	Lys	Arg	His	Ile	Cys	Asp	Ala	Asn	Lys	Glu	Gly	Met	Phe
								65	70		75			80	

Leu	Phe	Arg	Ala	Ala	Arg	Lys	Leu	Arg	Gln	Phe	Leu	Lys	Met	Asn	Ser
									85	90			95		

Thr	Gly	Asp	Phe	Asp	Leu	His	Leu	Leu	Lys	Val	Ser	Glu	Gly	Thr	Thr
									100	105			110		

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Ile Leu Leu Asn Cys Thr Gly Gln Val Lys Gly Arg Lys Pro Ala Ala
115 120 125

Leu Gly Glu Ala Gln Pro Thr Lys Ser Leu Glu Glu Asn Lys Ser Leu
130 135 140

Lys Glu Gln Lys Lys Leu Asn Asp Leu Cys Phe Leu Lys Arg Leu Leu
145 150 155 160

Gln Glu Ile Lys Thr Cys Trp Asn Lys Ile Leu Met Gly Thr Lys Glu
165 170 175

His Gly Gly Gly Ser Gly Gly Ser Gly Gly Ser Gly Ser
180 185 190

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
195 200 205

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
210 215 220

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
225 230 235 240

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
245 250 255

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
260 265 270

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
275 280 285

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
290 295 300

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
305 310 315 320

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
325 330 335

Cys Gln Ser Ile Ile Ser Thr Leu Thr
340 345

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<211> 333

<212> PRT

<213> artificial sequence (fusion murine IL7/linker/murine IL-2)

<400> 2

Met Phe His Val Ser Phe Arg Tyr Ile Phe Gly Ile Pro Pro Leu Ile
1 5 10 15

Leu Val Leu Leu Pro Val Thr Ser Ser Glu Cys His Ile Lys Asp Lys
20 25 30

Glu Gly Lys Ala Tyr Glu Ser Val Leu Met Ile Ser Ile Asp Glu Leu
35 40 45

Asp Lys Met Thr Gly Thr Asp Ser Asn Cys Pro Asn Asn Glu Pro Asn
50 55 60

Phe Phe Arg Lys His Val Cys Asp Asp Thr Lys Glu Ala Ala Phe Leu
65 70 75 80

Asn Arg Ala Ala Arg Lys Leu Lys Gln Phe Leu Lys Met Asn Ile Ser
85 90 95

Glu Glu Phe Asn Val His Leu Leu Thr Val Ser Gln Gly Thr Gln Thr
100 105 110

Leu Val Asn Cys Thr Ser Lys Glu Glu Lys Asn Val Lys Glu Gln Lys
115 120 125

Lys Asn Asp Ala Cys Phe Leu Lys Arg Leu Leu Arg Glu Ile Lys Thr
130 135 140

Cys Trp Asn Lys Ile Leu Lys Gly Ser Ile Gly Gly Gly Ser Gly
145 150 155 160

Gly Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu
165 170 175

Thr Leu Val Leu Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser
180 185 190

Ser Ser Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln
195 200 205

Gln Gln His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser
210 215 220

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Arg Met Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe
225 230 235 240

Lys Phe Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys
245 250 255

Leu Glu Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln
260 265 270

Ser Lys Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile
275 280 285

Arg Val Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys
290 295 300

Gln Phe Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp
305 310 315 320

Ile Ala Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln
325 330

<210> 3

<211> 330

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/human IL-15)

<400> 3

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

5/40

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Ser Met Arg Ile Ser Lys Pro His Leu
165 170 175

Arg Ser Ile Ser Ile Gln Cys Tyr Leu Cys Leu Leu Leu Asn Ser His
180 185 190

Phe Leu Thr Glu Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser
195 200 205

Ala Gly Leu Pro Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp
210 215 220

Leu Lys Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr
225 230 235 240

Leu Tyr Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met
245 250 255

Lys Cys Phe Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp
260 265 270

Ala Ser Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn
275 280 285

Ser Leu Ser Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys
290 295 300

Glu Glu Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val
305 310 315 320

His Ile Val Gln Met Phe Ile Asn Thr Ser
325 330

6/40

<211> 330

<212> PRT

<213> artificial sequence (fusion human IL-15/linker/human IL-2)

<400> 4

Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr
1 5 10 15

Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu Ala Gly Ile His
20 25 30

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala
35 40 45

Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile
50 55 60

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His
65 70 75 80

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln
85 90 95

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu
100 105 110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val
115 120 125

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile
130 135 140

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn
145 150 155 160

Thr Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly
165 170 175

Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala
180 185 190

Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln
195 200 205

Leu Gln Leu Glu His Leu Leu Asp Leu Gln Met Ile Leu Asn Gly

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210 215 220

Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys
225 230 235 240

Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu
245 250 255

Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser
260 265 270

Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val
275 280 285

Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr
290 295 300

Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr
305 310 315 320

Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
325 330

<210> 5

<211> 350

<212> PRT

<213> artificial sequence (fusion signal IL-2/ human IL-15/linker/human IL-2)

<400> 5

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser
20 25 30

Ile Gln Cys Tyr Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu
35 40 45

Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro
50 55 60

Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile
65 70 75 80

8/40

Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala, Thr Leu Tyr Thr Glu
85 90 95

Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu
 100 105 110

Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His
115 120 125

Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser
130 135 140

Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu
145 150 155 160

Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln
165 170 175

Met Phe Ile Asn Thr Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 180 185 190

Gly Gly Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala
195 . . . 200 . . . 205

Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr
210 215 220

Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met
225 230 235 240

Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met
245 250 255

Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His
260 265 270

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn
275 . . . 280 . . . 285

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
· 290 · 295 · 300

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe
305 310 315 320

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn
325 330 335

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Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
340 345 350

<210> 6

<211> 324

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/murine IL-15)

<400> 6

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
20 25 30

Glu Ala Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr
180 185 190

10/40

Leu Val Leu Leu Val Asn Ser Ala Gly Ala Asn Trp Ile Asp Val Arg
195 200 205

Tyr Asp Leu Glu Lys Ile Glu Ser Leu Ile Gln Ser Ile His Ile Asp
210 215 220

Thr Thr Leu Tyr Thr Asp Ser Asp Phe His Pro Ser Cys Lys Val Thr
225 230 235 240

Ala Met Asn Cys Phe Leu Leu Glu Leu Gln Val Ile Leu His Glu Tyr
245 250 255

Ser Asn Met Thr Leu Asn Glu Thr Val Arg Asn Val Leu Tyr Leu Ala
260 265 270

Asn Ser Thr Leu Ser Ser Asn Lys Asn Val Ala Glu Ser Gly Cys Lys
275 280 285

Glu Cys Glu Glu Leu Glu Glu Lys Thr Phe Thr Glu Phe Leu Gln Ser
290 295 300

Phe Ile Arg Ile Val Gln Met Phe Ile Asn Thr Ser Asp Tyr Lys Asp
305 310 315 320

Asp Asp Asp Lys

<210> 7

<211> 324

<212> PRT

<213> artificial sequence (fusion murine IL-15/linker/murine IL-2)

<400> 7

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Gly Ala Asn Trp Ile Asp Val Arg Tyr Asp Leu
20 25 30

Glu Lys Ile Glu Ser Leu Ile Gln Ser Ile His Ile Asp Thr Thr Leu
35 40 45

Tyr Thr Asp Ser Asp Phe His Pro Ser Cys Lys Val Thr Ala Met Asn
50 55 60

11/40

Cys Phe Leu Leu Glu Leu Gln Val Ile Leu His Glu Tyr Ser Asn Met
65 70 75 80

Thr Leu Asn Glu Thr Val Arg Asn Val Leu Tyr Leu Ala Asn Ser Thr
85 90 95

Leu Ser Ser Asn Lys Asn Val Ala Glu Ser Gly Cys Lys Glu Cys Glu
100 105 110

Glu Leu Glu Glu Lys Thr Phe Thr Glu Phe Leu Gln Ser Phe Ile Arg
115 120 125

Ile Val Gln Met Phe Ile Asn Thr Ser Asp Tyr Lys Asp Asp Asp Asp
130 135 140

Lys Gly Gly Gly Ser Gly Gly Gly Ser Met Tyr Ser Met Gln
145 150 155 160

Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu Leu Val Asn Ser Ala
165 170 175

Pro Thr Ser Ser Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln
180 185 190

Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu Met
195 200 205

Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys
210 215 220

Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr
225 230 235 240

Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg
245 250 255

His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala
260 265 270

Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys Gly
275 280 285

Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr Val
290 295 300

Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser
305 310 315 320

12/40

Thr Ser Pro Gln

<210> 8

<211> 361

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/human pro IL-18)

<400> 8

Met	Tyr	Arg	Met	Gln	Leu	Leu	Ser	Cys	Ile	Ala	Leu	Ser	Leu	Ala	Leu
1				5				10						15	

Val	Thr	Asn	Ser	Ala	Pro	Thr	Ser	Ser	Ser	Thr	Lys	Lys	Thr	Gln	Leu
	20					25					30				

Gln	Leu	Glu	His	Leu	Leu	Leu	Asp	Leu	Gln	Met	Ile	Leu	Asn	Gly	Ile
	35						40					45			

Asn	Asn	Tyr	Lys	Asn	Pro	Lys	Leu	Thr	Arg	Met	Leu	Thr	Phe	Lys	Phe
	50				55				60						

Tyr	Met	Pro	Lys	Lys	Ala	Thr	Glu	Leu	Lys	His	Leu	Gln	Cys	Leu	Glu
65					70				75				80		

Glu	Glu	Leu	Lys	Pro	Leu	Glu	Glu	Val	Leu	Asn	Leu	Ala	Gln	Ser	Lys
	85					90						95			

Asn	Phe	His	Leu	Arg	Pro	Arg	Asp	Leu	Ile	Ser	Asn	Ile	Asn	Val	Ile
	100				105						110				

Val	Leu	Glu	Leu	Lys	Gly	Ser	Glu	Thr	Thr	Phe	Met	Cys	Glu	Tyr	Ala
	115					120					125				

Asp	Glu	Thr	Ala	Thr	Ile	Val	Glu	Phe	Leu	Asn	Arg	Trp	Ile	Thr	Phe
	130				135				140						

Cys	Gln	Ser	Ile	Ile	Ser	Thr	Leu	Thr	Gly	Gly	Gly	Ser	Gly	Gly	
	145				150				155			160			

Gly	Gly	Ser	Gly	Gly	Ser	Met	Ala	Ala	Glu	Pro	Val	Glu	Asp		
	165					170			175						

Asn	Cys	Ile	Asn	Phe	Val	Ala	Met	Lys	Phe	Ile	Asp	Asn	Thr	Leu	Tyr
	180					185					190				

13/40

Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe Gly Lys
195 200 205

Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu
210 215 220

Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser
225 230 235 240

Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr
245 250 255

Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys
260 265 270

Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys
275 280 285

Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile
290 295 300

Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu
305 310 315 320

Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp
325 330 335

Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser
340 345 350

Ile Met Phe Thr Val Gln Asn Glu Asp
355 360

<210> 9

<211> 361

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/ human pro IL-18 K89A)

<400> 9

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

14/40

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Ser Met Ala Ala Glu Pro Val Glu Asp
165 170 175

Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr Leu Tyr
180 185 190

Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe Gly Lys
195 200 205

Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu
210 215 220

Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser
225 230 235 240

Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr
245 250 255

Ala Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys
260 265 270

Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys
275 280 285

15/40

Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile
290 295 300

Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu
305 310 315 320

Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp
325 330 335

Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser
340 345 350

Ile Met Phe Thr Val Gln Asn Glu Asp
355 360

<210> 10

<211> 325

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/mature human IL-18)

<400> 10

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

Gln Leu Glu His Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

16/40

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Gly Ser Tyr Phe Gly Lys Leu Glu Ser Lys
165 170 175

Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln
180 185 190

Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp
195 200 205

Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr Lys Asp Ser Gln
210 215 220

Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser
225 230 235 240

Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro
245 250 255

Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg
260 265 270

Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr
275 280 285

Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu
290 295 300

Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr
305 310 315 320

Val Gln Asn Glu Asp
325

<210> 11

<211> 325

<212> PRT

<213> artificial sequence (fusion human IL-2/linker/ mature human IL-18
K89A)

17/40

<400> 11

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Ser Gly Gly
145 150 155 160

Gly Gly Ser Gly Gly Ser Tyr Phe Gly Lys Leu Glu Ser Lys
165 170 175

Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln
180 185 190

Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp
195 200 205

Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr Ala Asp Ser Gln
210 215 220

Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser
225 230 235 240

Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro
245 250 255

18/40

Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg
260 265 270

Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr
275 280 285

Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu
290 295 300

Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr
305 310 315 320

Val Gln Asn Glu Asp
325

<210> 12

<211> 371

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/murine pro-IL-18)

<400> 12

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Thr Ala
20 25 30

Glu Ala Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

19/40

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Met Ala Ala Met Ser Glu Asp Ser Cys Val Asn Phe Lys
180 185 190

Glu Met Met Phe Ile Asp Asn Thr Leu Tyr Phe Ile Pro Glu Glu Asn
195 200 205

Gly Asp Leu Glu Ser Asp Asn Phe Gly Arg Leu His Cys Thr Thr Ala
210 215 220

Val Ile Arg Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln
225 230 235 240

Pro Val Phe Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro
245 250 255

Gln Thr Arg Leu Ile Ile Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly
260 265 270

Leu Ala Val Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser
275 280 285

Cys Lys Asn Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn
290 295 300

Ile Asp Asp Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro
305 310 315 320

Gly His Asn Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe
325 330 335

Leu Ala Cys Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys
340 345 350

Lys Asp Glu Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu
355 360 365

His Gln Ser
370

20/40

<210> 13

<211> 371

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/murine pro IL-18
K89A)

<400> 13

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu

1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Thr Ala
20 25 30Glu Ala Gln His Leu
35 40 45Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Ser Gly Gly
165 170 175Gly Gly Ser Met Ala Ala Met Ser Glu Asp Ser Cys Val Asn Phe Lys
180 185 190

21/40

Glu Met Met Phe Ile Asp Asn Thr Leu Tyr Phe Ile Pro Glu Glu Asn
195 200 205

Gly Asp Leu Glu Ser Asp Asn Phe Gly Arg Leu His Cys Thr Thr Ala
210 215 220

Val Ile Arg Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln
225 230 235 240

Pro Val Phe Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro
245 250 255

Gln Thr Arg Leu Ile Ile Tyr Met Tyr Ala Asp Ser Glu Val Arg Gly
260 265 270

Leu Ala Val Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser
275 280 285

Cys Lys Asn Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn
290 295 300

Ile Asp Asp Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro
305 310 315 320

Gly His Asn Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe
325 330 335

Leu Ala Cys Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys
340 345 350

Lys Asp Glu Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu
355 360 365

His Gln Ser
370

<210> 14

<211> 336

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/ mature murine IL-18)

<400> 14

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

22/40

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala
20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg
180 185 190

Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe
195 200 205

Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg
210 215 220

Leu Ile Ile Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly Leu Ala Val
225 230 235 240

Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn
245 250 255

Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp
260 265 270

23/40

Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn
275 280 285

Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys
290 295 300

Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu
305 310 315 320

Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser
325 330 335

<210> 15

<211> 336

<212> PRT

<213> artificial sequence (fusion murine IL-2/linker/mature murine IL-18
K89A)

<400> 15

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Thr Ala
20 25 30

Glu Ala Gln His Leu
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp
130 135 140

24/40

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Ser Gly Gly
165 170 175

Gly Gly Ser Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg
180 185 190

Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe
195 200 205

Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg
210 215 220

Leu Ile Ile Tyr Met Tyr Ala Asp Ser Glu Val Arg Gly Leu Ala Val
225 230 235 240

Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn
245 250 255

Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp
260 265 270

Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn
275 280 285

Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys
290 295 300

Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu
305 310 315 320

Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser
325 330 335

<210> 16

<211> 347

<212> PRT

<213> artificial sequence (fusion human IL-21/linker/ human IL-2)

<400> 16

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu
1 5 10 15

25/40

Ala Thr Ser Cys Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala
20 25 30

Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser Asn Phe Gln
35 40 45

Gln Pro Tyr Ile Thr Asn Arg Thr Phe Met Leu Ala Lys Glu Ala Ser
50 55 60

Leu Ala Asp Asn Asn Thr Asp Val Arg Leu Ile Gly Glu Lys Leu Phe
65 70 75 80

His Gly Val Ser Met Ser Glu Arg Cys Tyr Leu Met Lys Gln Val Leu
85 90 95

Asn Phe Thr Leu Glu Glu Val Leu Phe Pro Gln Ser Asp Arg Phe Gln
100 105 110

Pro Tyr Met Gln Glu Val Val Pro Phe Leu Ala Arg Leu Ser Asn Arg
115 120 125

Leu Ser Thr Cys His Ile Glu Gly Asp Asp Leu His Ile Gln Arg Asn
130 135 140

Val Gln Lys Leu Lys Asp Thr Val Lys Lys Leu Gly Glu Ser Gly Glu
145 150 155 160

Ile Lys Ala Ile Gly Glu Leu Asp Leu Leu Phe Met Ser Leu Arg Asn
165 170 175

Ala Cys Ile Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
180 185 190

Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu
195 200 205

Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr
210 215 220

Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn
225 230 235 240

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe
245 250 255

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys
260 265 270

26/40

Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln
275 280 285

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn
290 295 300

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu
305 310 315 320

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile
325 330 335

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
340 345

<210> 17

<211> 325

<212> PRT

<213> artificial sequence '(fusion murine IL-21/linker/murine IL-2)

<400> 17

Met Glu Arg Thr Leu Val Cys Leu Val Val Ile Phe Leu Gly Thr Val
1 5 10 15

Ala His Lys Ser Ser Pro Gln Gly Pro Asp Arg Leu Leu Ile Arg Leu
20 25 30

Arg His Leu Ile Asp Ile Val Glu Gln Leu Lys Ile Tyr Glu Asn Asp
35 40 45

Leu Asp Pro Glu Leu Leu Ser Ala Pro Gln Asp Val Lys Gly His Cys
50 55 60

Glu His Ala Ala Phe Ala Cys Phe Gln Lys Ala Lys Leu Lys Pro Ser
65 70 75 80

Asn Pro Gly Asn Asn Lys Thr Phe Ile Ile Asp Leu Val Ala Gln Leu
85 90 95

Arg Arg Arg Leu Pro Ala Arg Arg Gly Gly Lys Lys Gln Lys His Ile
100 105 110

Ala Lys Cys Pro Ser Cys Asp Ser Tyr Glu Lys Arg Thr Pro Lys Glu

27/40

115

120

125

Phe Leu Glu Arg Leu Lys Trp Leu Leu Gln Lys Met Ile His Gln His
130 135 140

Leu Ser Gly Gly Gly Ser Gly Gly Gly Ser Met Tyr Ser Met
145 150 155 160

Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu Leu Val Asn Ser
165 170 175

Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala Glu Ala Gln Gln
180 185 190

Gln Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu
195 200 205

Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu
210 215 220

Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala
225 230 235 240

Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu
245 250 255

Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp
260 265 270

Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys
275 280 285

Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr
290 295 300

Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile
305 310 315 320

Ser Thr Ser Pro Gln
325

<210> 18

<211> 334

<212> PRT

<213> artificial sequence (fusion human IFN-g/linker/human IL-2)

28/40

<400> 18

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu
1 5 10 15

Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu
20 25 30

Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn
35 40 45

Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp
50 55 60

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe
65 70 75 80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile
85 90 95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg
100 105 110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val
115 120 125

Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser
130 135 140

Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg
145 150 155 160

Gly Arg Arg Ala Ser Gln Gly Gly Gly Ser Gly Gly Gly Ser
165 170 175

Gly Gly Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala
180 185 190

Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Thr
195 200 205

Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met
210 215 220

Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met
225 230 235 240

29/40

Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His
245 250 255

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn
260 265 270

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser
275 280 285

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe
290 295 300

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn
305 310 315 320

Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr
325 330

<210> 19

<211> 334

<212> PRT

<213> artificial sequence (fusion murine IFN-g/linker/murine IL-2)

<400> 19

Met Asn Ala Thr His Cys Ile Leu Ala Leu Gln Leu Phe Leu Met Ala
1 5 10 15

Val Ser Gly Cys Tyr Cys His Gly Thr Val Ile Glu Ser Leu Glu Ser
20 25 30

Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser
35 40 45

Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys
50 55 60

Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val
65 70 75 80

Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser
85 90 95

His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala
100 105 110

30/40

Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln Arg
115 120 125

Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu Pro Glu
130 135 140

Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Gly Gly Gly Ser
145 150 155 160

Gly Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr
165 170 175

Leu Thr Leu Val Leu Leu Val Asn Ser Ala Pro Thr Ser Ser Thr
180 185 190

Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln
195 200 205

Gln Gln Gln His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu
210 215 220

Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr
225 230 235 240

Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln
245 250 255

Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr
260 265 270

Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn
275 280 285

Ile Arg Val Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu
290 295 300

Cys Gln Phe Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg
305 310 315 320

Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln
325 330

<210> 20

<211> 26

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-2)

<400> 20
cggaattcca cagtgacctc aagtcc 26

<210> 21
<211> 24
<212> DNA
<213> artificial sequence (antisense primer for cloning murine IL-2)

<400> 21
gggttacccc ttatgtgttg taag 24

<210> 22
<211> 34
<212> DNA
<213> artificial sequence (sense primer for cloning variant N88G of murine IL-2)

<400> 22
gagaatttca tcagcggtat cagagtaact gttg 34

<210> 23
<211> 34
<212> DNA
<213> artificial sequence (antisense primer for cloning variant N88G of murine IL-2)

<400> 23
caacagttac tctgataccg ctgatgaaat tctc 34

<210> 24
<211> 34
<212> DNA
<213> artificial sequence (sense primer for cloning variant N88R of murine IL-2)

<400> 24
gagaatttca tcagccgtat cagagtaact gttg 34

32/40

<210> 25
<211> 34
<212> DNA
<213> artificial sequence (antisense primer for cloning variant N88R of murine IL-2)

<400> 25
caacagttac tctgatacgg ctgatgaaat tctc 34

<210> 26
<211> 43
<212> DNA
<213> artificial sequence (sense primer for cloning variant Q126M of murine IL-2)

<400> 26
ggagatggat agccttctgt atgaggcatca tctcaacaag ccc 43

<210> 27
<211> 43
<212> DNA
<213> artificial sequence (antisense primer for cloning variant Q126M of murine IL-2)

<400> 27
gggcttgttg agatgatgct catacagaag gctatccatc tcc 43

<210> 28
<211> 27
<212> DNA
<213> artificial sequence (sense primer for cloning variant D20I of murine IL-2)

<400> 28
gagcagctgt tgatgatcct acaggag 27

<210> 29

33/40

<211> 27

<212> DNA

<213> artificial sequence (antisense primer for cloning variant D20I of murine IL-2)

<400> 29

ctcctgttagg atcatcaaca gctgctc

27

<210> 30

<211> 35

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-7)

<400> 30

ccgctcgagc ggatgttcca tgtttcttt agata

35

<210> 31

<211> 33

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-7)

<400> 31

cggggtaccc cgttatatac tgcccttcaa aat

33

<210> 32

<211> 32

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-18)

<400> 32

ccgctcgagc ggatggctgc catgtcagaa ga

32

<210> 33

<211> 43

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-18)

34/40

<400> 33
cgggttaccc cgcttaacttt gatgtaagtt agtgagagtgc aac 43

<210> 34
<211> 43
<212> DNA
<213> artificial sequence (sense primer for cloning variant K89A of murine IL-18)

<400> 34
ccagactgtat aatacatgt tacgcagaca gtgaagtaag agg 43

<210> 35
<211> 43
<212> DNA
<213> artificial sequence (antisense primer for cloning variant K89A of murine IL-18)

<400> 35
cctcttactt cactgtctgc gtacatgtat attatcagtc tgg 43

<210> 36
<211> 50
<212> DNA
<213> artificial sequence (sense primer for cloning mature murine IL-18)

<400> 36
ggggaggcg gttcaggcg aggtggctct aactttggcc gacttcactg 50

<210> 37
<211> 31
<212> DNA
<213> artificial sequence (antisense primer for cloning mature murine IL-18)

<400> 37
ctaactttga tgtaagttag tgagagtgaa c 31

35/40

<210> 38

<211> 32

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-21)

<400> 38

ccgctcgagc ggatggagag gacccttgtc tg

32

<210> 39

<211> 37

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-21)

<400> 39

cgggttaccc cgctaggaga gatgctgatg aatcatc

37

<210> 40

<211> 32

<212> DNA

<213> artificial sequence (sense primer for cloning murine IL-15)

<400> 40

ccgctcgagc ggatgtacag catgcagctc gc

32

<210> 41

<211> 31

<212> DNA

<213> artificial sequence (antisense primer for cloning murine IL-15)

<400> 41

cgggttaccc cgctacttgt catcgctgtc c

31

<210> 42

<211> 32

<212> DNA

<213> artificial sequence (primer 5' for generating the mIL2/IL18 fusion)

<400> 42
ccgctcgagc ggatgtacag catgcagctc ga 32

<210> 43

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the lIL2/IL18 fusion)

<400> 43
ggtgtggcg gttcaggcg aggtggctct atggctgccatgtcagaaga 50

<210> 44

<211> 50

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL2/IL18 fusion)

<400> 44
agagccacct ccgcctgaac cgccctccacc ttgagggctt gttgagatga 50

<210> 45

<211> 49

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL18/IL2 fusion)

<400> 45
ggtgtggcg gttcaggcg aggtggctct atgtacagca tgcagctcg 49

<210> 46

<211> 60

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL18/IL2 fusion)

<400> 46

37/40

agagccacct ccgcctgaac cgccctccacc actttgatgt aagttagtga gagtgaacat 60

<210> 47

<211> 31

<212> DNA

<213> artificial sequence (3' primer for generating the mIL18/IL2 fusion)

<400> 47
cgggttaccc cggttatttag gggttggta g 31

<210> 48

<211> 50

<212> DNA

<213> artificial sequence for generating the mIL2/mature IL18 fusion)

<400> 48
ggtgttggcg gttcaggcg aggtggctct aactttggcc gacttcactg 50

<210> 49

<211> 31

<212> DNA

<213> artificial sequence (3' primer for generating the mIL2/ mature IL18 fusion)

<400> 49
ctaactttga tgtaagttag tgagagtgaa c 31

<210> 50

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IL7 fusion)

<400> 50
ggtgttggcg gttcaggcg aggtggctct atgttccatg tttcttttag 50

<210> 51

<211> 49

38/40

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL7/IL2 fusion)

<400> 51
agagccacct ccgcctgaac cgccctccacc tatactgccc ttcaaaatt 49

<210> 52

<211> 50

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IL21 fusion)

<400> 52
ggtgtggaggcg gttcaggcg aggtggctct atggagagga cccttgcgtg 50

<210> 53

<211> 52

<212> DNA

<213> artificial sequence (3' linker primer for generating the mIL21/IL2 fusion)

<400> 53
agagccacct ccgcctgaac cgccctccacc ggagagatgc tgatgaatca tc 52

<210> 54

<211> 55

<212> DNA

<213> artificial sequence (5' linker primer for generating the mIL2/IFNg fusion)

<400> 54
ggtgtggaggcg gttcaggcg aggtggctct atgaacgcta cacactgcat ctgg 55

<210> 55

<211> 33

<212> DNA

<213> artificial sequence for generating the mIL2/IFNg fusion)

<400> 55
cgggtaccc cgtcagcgc gactccttt ccg 33

<210> 56
<211> 37
<212> DNA
<213> artificial sequence (5' primer for cloning the mIFNg/IL2 fusion)

<400> 56
ccgctcgagc ggatgaacgc tacacactgc atcttgg 37

<210> 57
<211> 49
<212> DNA
<213> artificial sequence (3' linker primer for generating the mIFNg/IL2 fusion)

<400> 57
agagccacct ccgcctgaac cgccctccacc gcagcgactc cttttccgc 49
<210> 58
<211> 50
<212> DNA
<213> artificial sequence (5' linker primer for generating the mIL2/IL15 fusion)

<400> 58
ggtgaggcg gttcaggcg aggtggctct atgtacagca tgcagctcg 50
<210> 59
<211> 49
<212> DNA
<213> artificial sequence (3' linker primer for generating the mIL15/IL2 fusion)

<400> 59

40/40

agagccacct ccgcctgaac cgccctccacc cttgtcatcg tcgtccttg

49